STIC Search Report
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STIC Database Tracking Number: 195101

TO: CECILIA JAISLE **Location: REM/4E78/5C18** **Art Unit: 1624** **Wednesday, July 19, 2006** **Case Serial Number: 10/824980**	**From: John DiNatale** **Location: Biotech-Chem Library** **REM-1B65** **Phone: (571)272-2557** **john.dinatale@uspto.gov**

Search Notes

Examiner JAISLE,

See attached results.

If you have any questions about this search feel free to contact me at any time.

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John DiNatale
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2557

ACCESS DB # 195101

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Scientific and Technical Information Center

SEARCH REQUEST FORM

10/824980

Requester's Full Name: Cecilia Jaisle Examiner # : 82613 Date: 7-10-06

Art Unit: 1624 Phone Number: 2-9931 Serial Number: ~~10/362,850~~

Location (Bldg/Room#): REM 4E78 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

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To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: see Bib Data Sheet

Inventors (please provide full names): _____

_____

Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

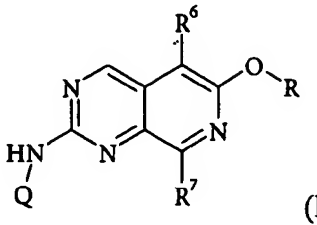
For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Call w/ any questions

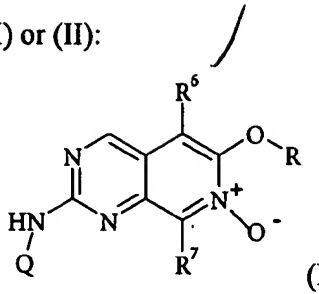
CLAIMS

The invention claimed is:

1. A compound having the Formula (I) or (II):



(I) or



(II),

or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

R is selected from:

(a) alkyl optionally-substituted with one to three of R^{17};

(b) cycloalkyl optionally substituted with one, two or three groups selected from R^{18}; and

(c) optionally-substituted aryl;

Q is selected from alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and alkyl substituted with one, two or three of halogen, cyano, $-OR^8$, $-SR^8$, $-C(=O)R^8$, $-C(O)_2R^8$, $-C(=O)NR^8R^9$, $-S(O)_pR^{10}$, $-C(O)_2NR^8R^9$, $-S(O)_2NR^8R^9$, $-NR^8R^9$, cycloalkyl, substituted cycloalkyl, heterocyclyl, and/or substituted heterocyclyl;

R^6 is hydrogen or lower alkyl;

R^7 is selected from hydrogen, alkyl, substituted alkyl, halogen, cyano, nitro, hydroxy, alkoxy, haloalkoxy, amino, alkylamino, and optionally-substituted cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^8 and R^9 are (i) independently selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, and substituted heterocyclyl; or (ii) when R^8 and R^9 are attached to the same nitrogen atom (as in $-C(O)_2NR^8R^9$, $-S(O)_2NR^8R^9$, and $-NR^8R^9$), R^8 and R^9 may be taken together to form an optionally-substituted heterocyclyl ring;

R^{10} is alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, or substituted heterocyclyl;

R^{17} is at each occurrence independently selected from halogen, haloalkoxy, haloalkyl, alkoxy, or optionally-substituted phenyl, benzyl, phenyloxy, benzyloxy, or cycloalkyl;

R^{18} is at each occurrence independently selected from alkyl, substituted alkyl, halogen, haloalkyl, haloalkoxy, cyano, alkoxy, acyl, alkoxycarbonyl, alkylsulfonyl, or optionally-substituted phenyl, phenyloxy, benzyloxy, cycloalkyl, heterocyclyl, or heteroaryl; and

p is 1 or 2.

2. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

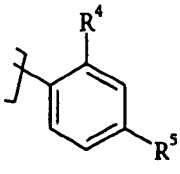
Q is selected from an alkyl or substituted alkyl having the formula $-C(R^1R^2R^3)$;

R^1, R^2 and R^3 are selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, $-(C_{1-4}alkylene)-S(O)_pR^{10}$, $-(C_{1-4}alkylene)-C(O)_2R^8$, cycloalkyl, cycloalkylalkyl, heterocyclyl, or heterocycloalkyl, wherein said cycloalkyl and heterocyclyl groups are, in turn, optionally substituted with up to one of R^{12} and up to one of R^{14}; and

R^{12} and R^{14} are independently selected where valence allows from C_{1-4}alkyl, hydroxy, oxo (=O), $-O(C_{1-4}alkyl)$, $-C(=O)H$, $-C(=O)(C_{1-4}alkyl)$, $-C(O)_2H$, $-C(O)_2(C_{1-4}alkyl)$, and $-S(O)_2(C_{1-4}alkyl)$.

3. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein R is phenyl substituted with one to two of lower alkyl, halogen, haloalkyl, haloalkoxy, cyano, and nitro.

4. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein R is:



; and

R^4 and R^5 are selected from halogen, haloalkyl, haloalkoxy, and cyano.

5. A compound according to claim 4, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

R^4 and R^5 are both halogen.

6. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein R^6 and R^7 are both hydrogen.

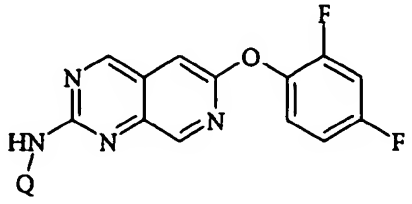
7. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein Q is C_{1-6}alkyl or hydroxy(C_{1-6}alkyl).

8. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein Q is an optionally-substituted C_{3-7}cycloalkyl or an optionally-substituted heterocyclic ring.

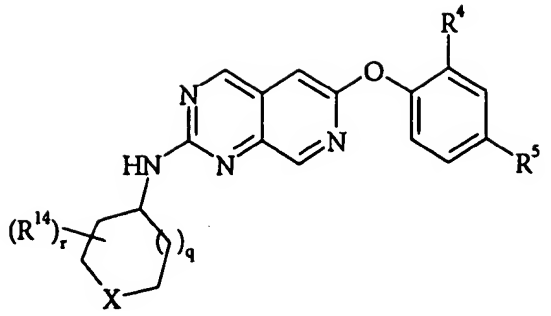
9. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

Q is cyclohexyl, piperidin-4-yl, or tetrahydropyran-4-yl, wherein each of said rings in turn is optionally-substituted with up to two of lower alkyl, –OH, $-C(O)_2(C_{1-4}$alkyl) and/or $-S(O)_2(CH_3)$.

10. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, having the formula:



11. A compound according to claim 1, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, having the formula:



wherein:

X is –O–, –C(=O)–, –N(R^{12a})–, or –CH(R^{12b})–;

R^{12a} is selected from hydrogen, C_{1-4}alkyl, –C(=O)R^{15}, –C(O)$_2R^{15}$, and –S(O)$_2$(C_{1-4}alkyl);

R^{12b} is selected from hydrogen, C_{1-4}alkyl, –OR^{15}, –C(=O)R^{15}, –C(O)$_2R^{15}$, and –S(O)$_2$(C_{1-4}alkyl);

R^{14} is selected from C_{1-4}alkyl, oxo (=O), –OR^{15}, –C(=O)R^{15}, –C(O)$_2R^{15}$, and –S(O)$_2$(C_{1-4}alkyl);

R^{15} is selected from hydrogen and C_{1-4}alkyl;

q is 0 or 1; and

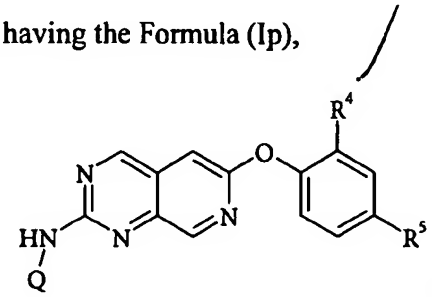
r is 0, 1 or 2.

12. A compound according to claim 11, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

R^4 and R^5 are both fluoro.

13. A compound according to claim 11, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein X is –NR^{12a}–, R^{12a} is -S(O)$_2$(C_{1-4}alkyl), and *q* is 1.

14. A compound having the Formula (Ip),



(Ip)

or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein:

Q is alkyl, substituted alkyl or an optionally-substituted cycloalkyl or heterocyclyl, provided Q is not arylalkyl or heteroarylalkyl ; and

R^4 and R^5 are both halogen;

15. A compound according to claim 14, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein R^4 and R^5 are both fluoro.

16. A compound according to claim 14, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein Q is an optionally-substituted monocyclic cycloalkyl or heterocyclyl ring.

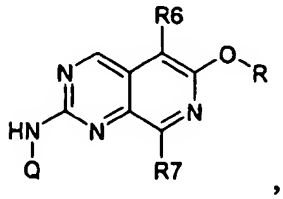
17. A pharmaceutical composition comprising a therapeutically effective amount of compound according to Claim 1 in combination with a pharmaceutically-acceptable excipient.

18. A method for treating a p38-mediated disorder in a patient comprising administering to the patient in need of such treatment, an effective amount of a compound according to Claim 1.

19. The method of Claim 18, wherein the p38-mediated disorder is selected from the group consisting of arthritis, Crohn's disease, Alzeihmer's disease, adult respiratory distress syndrome, chronic obstructive pulmonary disease, asthma, stroke, sepsis, myocardial infarction, and spondylitis.

20. A method for inhibiting p38 kinase in a mammal comprises administering to said mammal a compound according to claim 1.

21. A process for preparing a compound of formula (I)



,

wherein R is selected from:

(a) alkyl optionally-substituted with one to three of R^{17};

(b) cycloalkyl optionally substituted with one, two or three groups selected from R^{18}; and

(c) optionally-substituted aryl;

Q is selected from alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and alkyl substituted with one, two or three of halogen, cyano, $-OR^8$, $-SR^8$, $-C(=O)R^8$, $-C(O)_2R^8$, $-C(=O)NR^8R^9$, $-S(O)_pR^{10}$, $-C(O)_2NR^8R^9$, $-S(O)_2NR^8R^9$, $-NR^8R^9$, cycloalkyl, substituted cycloalkyl, heterocyclyl, and/or substituted heterocyclyl;

R^6 is hydrogen or lower alkyl;

R^7 is selected from hydrogen, alkyl, substituted alkyl, halogen, cyano, nitro, hydroxy, alkoxy, haloalkoxy, amino, alkylamino, and optionally-substituted cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^8 and R^9 are (i) independently selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, and substituted heterocyclyl; or (ii) when R^8 and R^9 are attached to the same nitrogen atom, R^8 and R^9 may be taken together to form an optionally-substituted heterocyclyl ring;

R^{10} is alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, or substituted heterocyclyl;

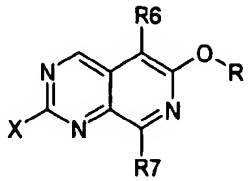
R^{17} is at each occurrence independently selected from halogen, haloalkoxy, haloalkyl, alkoxy, or optionally-substituted phenyl, benzyl, phenyloxy, benzyloxy, or cycloalkyl;

R^{18} is at each occurrence independently selected from alkyl, substituted alkyl, halogen, haloalkyl, haloalkoxy, cyano, alkoxy, acyl, alkoxycarbonyl, alkylsulfonyl, or optionally-substituted phenyl, phenyloxy, benzyloxy, cycloalkyl, heterocyclyl, or heteroaryl; and

p is 1 or 2;

wherein said process comprises:

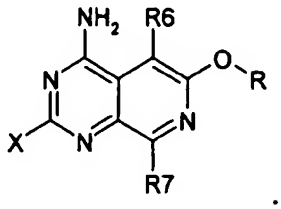
(i) providing a compound of formula (8); and



where X is a leaving group; and

(ii) contacting said compound of formula (8) with a compound of the formula NH_2Q in a polar, aprotic solvent.

22. The process of claim 21, wherein said compound of formula (8) is provided by treating a compound of formula (7) with *t*-butylnitrite:



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Bib Data Sheet

CONFIRMATION NO. 7688

SERIAL NUMBER	FILING OR 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/824,980	04/15/2004 RULE	514	1624	R0164B-REG

APPLICANTS

Nolan James Dewdney, San Jose, CA;
David Michael Goldstein, San Jose, CA;

**** CONTINUING DATA ***************************

This appln claims benefit of 60/463,229 04/16/2003

**** FOREIGN APPLICATIONS *********************

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 06/26/2004

Foreign Priority claimed	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ yes ☐ no	CA	0	22	3
35 USC 119 (a-d) conditions met ☐ yes ☐ no ☐ Met after Allowance				
Verified and Acknowledged _____ Examiner's Signature Initials				

ADDRESS
24372

TITLE

Substituted 7-azaquinazoline compounds useful as p38 kinase inhibitors

FILING FEE RECEIVED		
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Biotech-Chem Library

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Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

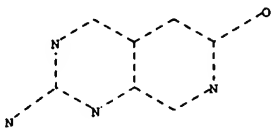
- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

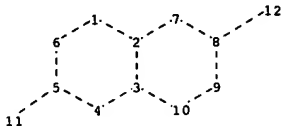
Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.

C:\Program Files\Stnexp\Queries\10_824980\jai-b.str

structure "L3"





ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
11 12
chain bonds :
5-11 8-12
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 7-8 8-9 8-12 9-10

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS

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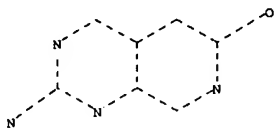

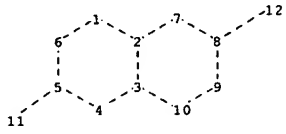

chain nodes :
    11 12
ring nodes :
    1 2 3 4 5 6 7 8 9 10
chain bonds :
    5-11 8-12
ring bonds :
    1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
    1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 7-8 8-9 8-12 9-10
isolated ring systems :
    containing 1 :

Connectivity :
    1:2 E exact RC ring/chain 4:2 E exact RC ring/chain 6:2 E exact RC ring/chain
    11:2 M minimum RC ring/chain
Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
    12:Atom

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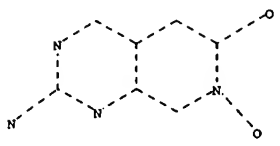
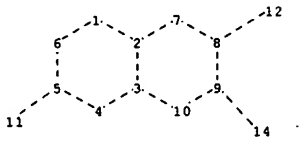
structure "L22"





chain nodes :
    11 12 14
ring nodes :
    1 2 3 4 5 6 7 8 9 10
chain bonds :
    5-11 8-12 9-14
ring bonds :
    1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
    1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 7-8 8-9 8-12 9-10 9-14

Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
    12:Atom 14:CLASS